mice of the publication are +/+ for the mouse elastin gene (these being the wild type endogenous genes) and they cannot be +/- or -/- for the mouse elastin gene. It is asserted that the mice of the Sechler et al. publication do not meet the limitations of claims 2 and 4 because these claims require that there be no functioning elastin gene present. The mice of the Sechler et al. publications have two functioning wild type elastin genes. Claims 2 and 4 are for a mouse and mouse cell comprising a genome with no functional elastin gene, therefore it is asserted that those claims are not anticipated by Sechler et al. because Sechler et al teach mice with two functional elastin genes.

It is emphasized that "genome" is inclusive of all DNA in the cell, not only a separate portion of what is present. Consequently, the focus must be on all genes present in the Sechler et al. mice, including the normal chromosomal genes, and not solely on the transgenes.

In view of the above arguments, it is requested that the 35 U.S.C. § 102(b) rejection of claims 2 and 4 be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-4 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Sechler et al., in view of Wydner et al.

Claims 1 and 3 have been amended to limit them to only one functional nontransgenic elastin gene. Claims 1 and 3 are directed to a mouse or mouse cell comprising solely one functional elastin gene and either one nonfunctional or no second elastin gene. The mice of claims 1 and 3 require that there be one and only one functioning elastin gene whereas the Sechler et al. publication teaches mice that have two functioning elastin mouse genes. It is therefore asserted that mice of the Sechler publication do not teach the mice of claims 1 and 3.

The Office Action states that the Sechler et al. publication does not teach the availability of mouse elastin gene for making a mouse containing mutated mouse elastin gene, but asserts that the Wydner et al. publication teaches the complete cDNA sequence of mouse elastin gene. The Sechler et al. publication does not suggest to substitute the rat elastin gene. The addition of the Wydner et al. publication does not add to the obviousness. The Wydner et al. publication teaches the sequence of the mouse elastin gene. The Wydner et al. publication does not teach a mouse or mouse cell comprising a genome comprising a functional elastin gene and either one nonfunctional mouse elastin gene or no second elastin gene. The Wydner et al. reference simply

teaches the sequence of the mouse elastin gene. The combination of the two references does not teach making a mouse containing a mutated mouse elastin gene.

Claims 2 and 4 are directed to a mouse or mouse cell comprising a genome with no functional elastin gene. As stated earlier, the mice of the Sechler publication have two functioning elastin genes. The Wydner et al. publication teaches the cDNA sequence of the mouse elastin gene. The mice of claims 2 and 4 have no functional elastin gene. It would not have been obvious to one of ordinary skill in the art to combine the knowledge of these two references to create a mouse or mouse cell with no functional elastin gene.

Claims 5, 6, 9 and 10 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over Reitamo et al. in view of Sechler et al. and Wydner et al. Claim 5 is directed to a method to screen for drug candidates useful for treating humans with SVAS, hypertension, or atherosclerosis by using an ELN +/- mouse or human, wherein said drug candidates inhibit occlusion of arteries. Claim 6 is directed to a method to screen for drug candidates useful for treating humans with atherosclerosis, SVAS or essential hypertension by measuring activity of elastase in the presence of drugs wherein said drugs which inhibit elastase are said drug candidates. Claims 9 and 10 are directed to a method to screen for drug candidates useful for treating humans with SVAS, hypertension or atherosclerosis by using ELN +/- mouse or human, or ELN +/- mouse or human cells and by measuring the synthesis of elastin RNA and elastin, respectively.

The Reitamo et al. publication teaches generating transgenic mice expressing a human elastin promoter and a method of screening a compound which can stimulate the elastin promoter. The Examiner admits that Reitamo does not teach using ELN +/- mice or ELN -/- cells to screen drug candidates useful for treating atherosclerosis hypertension or SVAS in a human. But the Examiner asserts that the combination of the three references makes the Applicants' invention unpatentable. However, it is asserted by the Applicants that the combination of these references does not make the Applicants' invention unpatentable.

It is emphasized that the claimed invention is of an entirely different concept than that of the Sechler et al. publication. Applicants' invention involves mice with either no elastin or 50% of the normal amount of elastin, meaning they have a shortage of the wild type elastin. The

SVAS and other disorders discussed by the Applicant are due to a lack of synthesis of elastin (see the last paragraph on page 5 of the application). The Sechler et al. publication involves an entirely different type of invention. The Sechler et al. publication teaches mice with wild type elastin and a mutant elastin forming a complex structure (it is the merging of the wild type and the mutant elastin). The Sechler et al. publication teaches abnormalities which result from coexpression of normal elastin plus mutant elastin with the forms then coassembling. "Our reasoning behind the construction of several founder strains of transgenic mice was that the introduction of an exogenous tropoelastin gene containing a mutation would result in the synthesis of abnormal tropoelastin monomers that would be incorporated into the elastin together with the normal, endogenous mouse tropoelastin." Sechler et al., p. 150. This is very different from the claimed invention which involves a lack of synthesis of wild-type elastin.

In view of the above arguments, it is requested that the rejection of claims 5, 6, 9 and 10 Under 35 U.S.C. § 103 be withdrawn.

In view of the above arguments, it is submitted that the present claims satisfy the provisions of the patent statutes and are patentable over the prior art. Reconsideration of this application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned to expedite allowance of this application.

Respectfully submitted,

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